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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/824,134	04/03/2001	David Wallach	WALLACH=16A	2547

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/824,134	WALLACH ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,11 and 14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,11 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Accordingly, claims 1-7, 11, 14 are being examined.

The following are the remaining rejections.

The 112 second paragraph, the 112 first paragraph, written description and scope rejections are reinstated.

REJECTION UNDER 35 USC 112, SECOND PARAGRAPH

Rejection of claims 1-7, 11, 14 concerning the indefinite language "moderately stringent conditions" in claim 1 is reinstated.

In the response of 02/24/03, Applicant argues that US 5,026,636 defines moderate stringency as conditions that allow detection of sequences at least 75% homologous to the probe and that the conditions could be readily determined using a reference text for guidance. Applicant argues that claims of US 4,968,607 include the term "moderate stringency". Applicant recites Ausubel et al, 1987-1998, Current protocols in Molecular Biol, which teaches how to determine moderate stringency wash conditions, by calculating the decrease in temperature required using the correlation for decrease in Tm percent mismatch. Applicant argues that based on the teaching in the art, the scope of "moderate stringency" could be determined.

Applicant's arguments set forth in paper of 07/03/03 have been considered but are not deemed to be persuasive for the following reasons:

Since there is no definition of moderately stringent hybridization conditions is found in the specification, one cannot determine the metes and bound of the claimed invention.

Although some US patents use the language or define the language, or some references teach how to determine moderate stringency wash, the definition by another US patent would be just one of possible numerous reasonable interpretations of the claimed moderately stringent hybridization conditions, in view of the lack of definition of the term in the claimed application, and in view that moderate is a relative term. Concerning how to determine moderate stringency wash, this is not an enablement rejection.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

Rejection under 35 USC 112, first paragragh of claims 1-7, 11, 14 pertaining to **lack of a clear written description of the claimed a DNA sequence encoding an "analog" of the MORT-1 protein having the amino acid sequence of SEQ ID NO:2,** remains for reasons already of record in paper of 07/03/03.

Applicant argues in paper of 12/03/03 that binding to the intracellular domain of the FAS ligand receptor is both a physical property and a function. Applicant argues that binding alone is sufficient to establish the function of, for example, serving in affinity chromatography to isolate MORT-1 (p.7, last line of the first paragraph, in the response of 12/03/03). Applicant argues that the function of the protein or polypeptide encoded by the DNA of claim 1 may be any function disclosed in the specification. Applicant argues

that it is acceptable to show that one is in possession of a compound by identifying characteristics which includes physical properties.

Applicant recites the Written description guidelines which states that :

An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, ï.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

Applicant argues that the analog of claim 1(2) is defined by a complete or partial structure and other physical and/or chemical properties. Applicant argues that there is a partial structure because the DNA encoding it must be capable of hybridizing to the cDNA encoding SEQ ID NO:2 under moderately stringent conditions. Applicant argues that this combination of partial structure and physical and/ or chemical is sufficient to that Applicant was in possession of the claimed invention.

Applicant's arguments set forth in paper of 07/03/03 have been considered but are not deemed to be persuasive for the following reasons:

Contrary to Applicant's arguments, no one of skill in the art would reasonably conclude that Applicant had possession of the claimed DNA sequences encoding a genus of analogs of MORT-1 protein of SEQ ID NO:2 at the time of filing for the reasons of record. The claimed analog lacks definitive function which is correlated with a specific function.

Contrary to Applicant's arguments, binding to FAS-IC alone is not a definitive function, such that the function defines MORT-1. There is no teaching in the specification that would permit one of skill to predictably identify the species included in the claimed genus, and to distinguish between that which is claimed from that which is not claimed. Thus the specification does not provide a written description of the claimed invention, that would demonstrate that Applicant was in possession of the claimed invention at the time of filing.

In addition, concerning Applicant's assertion that function of the claimed analog of serving in affinity chromatography to isolate MORT-1, the encoded sequence consisting of amino acids 130-245 of SEQ ID NO:2 binds to FAS-IC, but does not bind to the MORT-1 protein of SEQ ID NO:2 (specification, p.36, line s4-5), and thus cannot be used for making affinity column to isolate MORT-1 protein.

Further, there is no correlation provided between the properties of "DNA sequences encoding sequences that bind to FAS-IC" and structure of "a DNA sequence that has the ability to hybridize to the cDNA encoding SEQ ID NO:2, under moderately stringent conditions", because there are proteins that bind to FAS-IC, such as FAS ligand, and antibodies to FAS-IC, but having a structure completely different from the disclosed amino acids 130-245 of MORT-1 of SEQ ID NO:2.

In other words, not only binding to FAS-IC is not a definitive function, there is no correlation between the properties of binding to FAS-IC and structure of a DNA sequence that has the ability to hybridize to the cDNA encoding SEQ ID NO:2, under moderately stringent conditions. The specification discloses only a single cDNA

sequence encoding the MORT-1 protein of SEQ ID NO:2, wherein the amino acids 130-245 of SEQ ID NO:2 bind to the intracellular domain of the FAS-ligand receptor. This is insufficient to establish a correlation between the property of binding to FAS-IC, which is shared by unrelated sequences, and structure of a DNA sequence that has the ability to hybridize to the cDNA encoding SEQ ID NO:2.

In addition, although a partial structure is implied in claim 1, by the recitation of a DNA sequence capable of hybridizing to the cDNA encoding SEQ ID NO:2 under moderately stringent conditions, said structure is undefined, and is not correlated with the ability to bind to FAS-IC, because any unrelated DNA sequence with unknown function could hybridize to a CDNA sequence encoding SEQ ID NO:2 under moderately stringent conditions, via a common fragment, wherein said fragment does not necessarily have to encode amino acids 130-245 of the MORT-1 protein of SEQ ID NO:2, a fragment necessary for binding to FAS receptor (specification, page 36). The language "DNA sequence capable of hybridizing to the cDNA encoding SEQ ID NO:2 under moderately stringent conditions" per se does not define that the sequence encodes the amino acids 130-245 of the MORT-1 protein of SEQ ID NO:2, a sequence necessary for binding to FAS-IC.

Thus, there is no correlation between structure and function for the claimed DNA sequence encoding an analog of MORT-1 protein of SEQ ID NO:2 in claim 1, that would allow one to distinguish between that which is claimed from that which is not claimed.

Moreover, the specification does not disclose a representative number of species of DNA sequences encoding an analog of MORT-1 protein, wherein which analog binds

to FAS-IC, and wherein which DNA sequence is capable of hybridizing to the cDNA encoding SEQ ID NO:2. The specification only discloses a single DNA sequence that encodes the amino acids 130-245 of the MORT-1 protein of SEQ ID NO:2, wherein said amino acid sequence is necessary for binding to FAS-IC.

For the reasons set forth previously and above, the claimed invention does not meet 112, first paragraph, written description requirement, and one would reasonably conclude that Applicant did not have possession of the claimed DNA sequences encoding a genus of analog of SEQ ID NO:2 at the time of filing.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

Rejection under 35 USC 112, first paragragh of claims 1-7, 11, 14, because while being enabled for a DNA sequence encoding the amino acid sequence of SEQ ID NO:2, **the specification lacks enablement for a DNA sequence encoding a fragment of MORT-1 protein which binds FAS-IC, or encoding an "analog" of the MORT-1 protein having the amino acid sequence of SEQ ID NO:2**, remains for reasons already of record in paper of 03/04/04.

In the brief of 03/04/04 Applicant argues that the Examiner states that Applicant has not taught how to make variants that are capable of hybridizing to the cDNA encoding SEQ ID NO:2 under moderately stringent conditions, such that those variants would bind to the intracellular domain of the FAS ligand receptor, and that determining which analogs binds FAS-IC would not entail undue experimentation, in view of Wands

analysis (p.15-20). Applicant argues that mutation method is routine in the art, and that screening is routine, and thus they do not amount to undue experimentation.

Applicant's arguments set forth in paper of 03/04/04 have been considered but are not deemed to be persuasive for the following reasons:

It is noted that the Examiner did not state that Applicant has not taught how to make variants that are capable of hybridizing to the cDNA encoding SEQ ID NO:2 under moderately stringent conditions, **such that those variants would bind to the intracellular domain of the FAS ligand receptor.**

Rather, the Examiner position is that Applicant has not taught how to make variants that are capable of hybridizing to the cDNA encoding SEQ ID NO:2 under moderately stringent conditions, **such that those variants would have the properties and function of the claimed polynucleotides encoding SEQ ID NO:2** (previous Office action of 03/04/04, page 3, fourth paragraph).

The specification discloses that MORT-1 binds to intracellular domain of FAS receptor, and thus is capable of modulating the function of the FFAS receptor, and that amino acids 1-117 are necessary for self association, and amino acids 130-245 are necessary for binding to FAS receptor (p. 1, first full paragraph, p.36). The specification further discloses that FAS receptor mediates cell death, and that monoclonal antibodies to FAS receptor could induce apoptotic cell death (p.3, second paragraph).

The specification also discloses that however, MORT-1 can activates cell cytotoxicity on its own (p. 1, first full paragraph). No disclosure concerning which fragment is responsible for activation of cell cytotoxicity is found in the specification.

It is noted that binding to a receptor does not necessarily mean that the receptor would be activated, because although there is certain plasticity in ligand-receptor interactions, the ligand has to have a certain binding stability, and has to have molecular configuration specificity, for example, a certain configuration for perfect fit into the receptor for activation of the receptor, like lock and key . For example, Zhang et al, 2005, Acta Pharmacoligica Sinica, 26(2): 171-176 teach that the effect of an estrogen ligand requires molecular configuration specificity of the ligand. Yoshikawa Noritada et al, Molecular endocrinology, May 2005, 19 (5):p1110-24, teach that for activation of the glucocorticoid receptor, stable conformational changes of the ligand binding domain, induced by binding of the receptor to the ligand seem to be necessary for activation of the receptor. Wilson I A et al, Current opinion in structural biology (ENGLAND) Dec 1999, 9 (6): p696-704, teach that erythropoietin receptor activation is dependent on the actual configuration of the receptor-ligand dimer assembly. Petry Renate et al, Journal of medicinal chemistry (United States) Feb 28 2002, 45 (5): p1026-34,teach that stabilization of a particular structural state of the receptor, and further induction of conformational rearrangements of the receptor by the ligand is necessary for receptor activation.

In view of the art, although one could screen for fragments of SEQ ID NO:2 that bind to FAS-IC, one cannot predict that amino acids 130-245 of SEQ ID NO:2, and variants thereof would activate the FAS receptor. For example, one cannot predict whether amino acids 130-245 of SEQ ID NO:2 would have the molecular configuration specificity required for FAS receptor activation, or would stabilize a certain particular

structural state of the FAS receptor or would induce certain conformational changes of the FAS receptor, that might be required for FAS receptor activation.

Thus **one would not know how to use the claimed DNA sequence encoding such fragments that bind to FAS-IC, nor MORT-1 analogs as claimed in claim 1**, and it would be undue experimentation for one of skill in the art to practice the claimed invention.

Further, the claimed analogs would not necessarily have the function and properties of polypeptide encoding SEQ ID NO:2, such as activation of cell cytotoxicity, because the specification does not disclose which fragments of SEQ ID NO:2 are responsible for such activation of cell cytotoxicity. **One would not know how to make the claimed analogs, such that they would have the function of the polypeptide encoding SEQ ID NO:2**, in view of the unpredictability of protein chemistry, as taught by Burgess et al, Lazar et al, Tao et al, and Gillies et al, all of record, and in view that such unpredictability would apply as well to DNA sequences which encode proteins.

It is noted that MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature ot the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In contrast, if little is

known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Given the unpredictability that the encoded fragment that binds FAS-IC, or the encoded analogs of MORT-1 protein would activate FAS receptor, and the unpredictability of protein chemistry, which applies as well to DNA sequences encoding proteins, the lack of adequate disclosure in the specification, and in view of the complex nature of the claimed invention, and little is known in the art about the claimed invention, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

MINH TAM DAVIS

May 18, 2005